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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/122,588	07/23/98	SEMPLE S	016303-00531

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EXAMINER	
SCHMIDT, M	
ART UNIT	**PAPER NUMBER**
1635	13

DATE MAILED: 06/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/122,588	Semple et al.
Examiner	**Group Art Unit**
Schmidt	1635

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Peri d for Response

A SHORTENED STATUTORY PERIOD FOR RESPONSE IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a response be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for response specified above is less than thirty (30) days, a response within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for response is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to respond within the set or extended period for response will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☒ Responsive to communication(s) filed on 3/14/00 & 11/22/99.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle,* 1935 C.D. 1 1; 453 O.G. 213.

Disp sition of Claims

☒ Claim(s) 62-83 is/are pending in the application.

Of the above claim(s)_____ is/are withdrawn from consideration.

☐ Claim(s)_____ is/are allowed.

☒ Claim(s) 62-83 is/are rejected.

☐ Claim(s)_____ is/are objected to.

☐ Claim(s)_____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on_____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on_____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)_____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:_____.

Attachment(s)

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s)._____

☐ Interview Summary, PTO-413

☐ Notice of References Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other_____

Office Action Summary

DETAILED ACTION

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. New claims 62-83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cells and methods of delivery and/or treatment involving the liposome containing a catalytic nucleic acid *in vitro*, does not reasonably provide enablement for application of such compositions to any biological system including any whole organism or cells there of for the same reasons of record as set forth for old claims 1-15, 17-20, 26, 35-37, 39-46, 49-59 and 61 in the Official action mailed 02/09/00 . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Applicant's arguments filed 11/22/99 have been fully considered but they are not persuasive.

The new claims 62-83 are drawn to methods of treating a neoplasia in a mammal comprising administering to a mammal a pharmaceutical composition comprising a polyethylene glycol (PEG)-ceramide conjugate, a lipid, a nucleic acid catalyst such that a therapeutic result is obtained.

Applicant responds on pages 6-12 of the response filed 11/22/99 in two parts: (1) "One of skill would have had no difficulty making and using the claimed invention", and (2) "Operability of claimed invention."

In the first part, applicants point out parts of the specification which teach working examples of preparation of the PEG-ceramide, lipid, and nucleic acid catalyst formulations and examples of *in vivo* application of the claimed constructs.

In response, examiner acknowledges that the specification provides some evidence of construction of certain concentrations of PEG-ceramide, lipid and nucleic acid catalyst formulations, and that those such concentrations as taught in the specification were known in the art (see the previous rejection under 35 USC 103 in the action mailed 5/27/99). Further, it was noted that the specification teaches some evidence of success of the taught compositions in mice. Note that the previous rejection specifies that "One of skill in the art would not accept on its face the successful delivery, and further treatment effects of the claimed catalyst compositions in whole organisms *other than mice*..." Therefore, the rejection was focused on the lack of correlation between the teachings of the specification and the scope of the claimed invention for administration of any such compositions to any whole organism as broadly claimed.

Applicants further respond that "Applicant's interpret the Examiner's 112, first paragraph rejection as relating in essence to the utility of the claimed invention, ie., whether the invention actually works as claimed." However, the rejection was not based on the utility per se, since this is not a 35 USC 101 rejection. Instead the rejection was made on the amount of undue

experimentation required for one skilled in the art to make and use the invention. The weight of balance of the factors considered for such undue experimentation (see MPEP 2164.01(a)) was found to cause one skilled in the art to necessarily practice an undue amount of experimentation to make and use the claimed invention for administration of the breadth of claimed constructs in any whole organism for the therapeutic functions claimed.

Applicants subsequently address the factors listed as unpredictable in the previous rejection mailed 5/27/99: (1) stability of the ribozyme liposome composition *in vivo* in any whole organism other than mice, (2) effective delivery to the whole organism and specificity to the target tissues, (3) dosage and toxicity, and (4) entry of molecule into the cell and effective action therin marked by visualization of the desired treatment effects via the catalytic molecule.

Applicant responds that case law teaches that animal data is sufficient for efficacy in humans. However, in general, the test is whether there is a correlation between what was taught and the scope of the claimed invention. In the instant case, there is not a clear correlation between the teaching of VEGF-R-1 (with specific liposome formulations) expressed ribozymes in hyperoxic neonatal mice and the Lewis Lung Carcinoma Model with the breath of therapeutic functions claimed with any catalytic nucleic acid molecule having any liposome formulation for treatment in any whole organism. The additional prophetic evidence in the specification would not render the administration of the breadth of possible compositions predictable to one skilled in the art for the therapeutic effects claimed.

Specifically, the unpredictability in the art for these factors is well-known and the success with one therapeutic ribozyme or gene does not correlate with success for other such compositions in any whole organism. For instance, Branch was cited to teach the unpredictablity of design of antisense and ribozymes to a known target as unpredictable. The problems compound when such nucleic acid compositions are then administered *in vivo*. Routes of administration are also known in the art to vary the success of therapeutically administered nucleic acid compositions. Therefore, despite the teaching in the specification of certain *in vivo* successes of VEGF-R-1 in mice, such evidence does not widely correlate to predictable success for the scope of the therapeutic effects in the claimed invention.

Therefore, the new claims do not overcome a *prima facie* case of lack of enablement for the claimed invention.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to *Mary M. Schmidt*, whose telephone number is (703) 308-4471.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *George Elliott, Ph.D.* may be reached at (703) 308-4003.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

M. M. Schmidt
June 2, 2000

George C. Elliott, Ph.D.
Supervisory Patent Examiner
Technology Center 1600